BEH. 410 - March 2003

Problem set # 2 - SOLUTION

Problem 1 - Microtubule structure

- Flexural rigidity $\kappa_f = Y . I$, where $\begin{cases} Y \text{ is the microtubule's Young modulus} \\ \quad \text{take } Y = 10^9\ J.m^{-3} \ \text{(Boal p. 53)} \\ I \text{ moment of inertia} \end{cases}$

$$\left.\begin{array}{l} - \text{hollow tube} \quad \left.\begin{array}{l} R = 14\ nm \\ R_i = 11.5\ nm \end{array}\right\} \quad I_h = \frac{\pi}{4}\left(R^4 - R_i^{\,4}\right) = 1.64 \cdot 10^{-32}\ m^4 \\ - \text{solid tube} \quad \left.\begin{array}{l} R = 14\ nm \\ R_i = 0\ nm \end{array}\right\} \quad I_s = \frac{\pi}{4} R^4 = 3.02 \cdot 10^{-32}\ m^4 \end{array}\right\} \quad \frac{I_s}{I_h} = 1.84$$

- Mass ratio of a microtubule of density $\rho_m = 10^3\ kg\ m^{-3}$ and length L

$$\left.\begin{array}{l} - \text{hollow tube} \quad m_h = \rho_m . \pi . (R^2 - R_i^{\,2}) . L \\ - \text{solid tube} \quad m_s = \rho_m . \pi . R^2 . L \end{array}\right\} \quad \frac{m_s}{m_h} = \frac{1}{1 - \frac{R_i^{\,2}}{R^2}} = 3.07$$

While a hollow microtubule has only around one third of the mass of a solid microtubule, it has over half its rigidity. The most efficient way for a cell to gain rigidity is to use many hollow microtubules rather than one solid one, it makes better use of the number of proteins required, of its resources in proteins.

Problem 3 - Properties of ideal chains

From Boal's chapter 2 p. 44-46, we have, for an ideal chain in 3-D:

$$p^*(r) = 4\pi r^2 \left(2\pi\sigma^2\right)^{-3/2} \exp\left(\frac{-r^2}{2\sigma^2}\right) \quad \text{with } \sigma^2 = \frac{Nb^2}{3}.$$

$$\langle r_{ee}\rangle = \frac{\int_{r_{ee}=0}^{+\infty} r_{ee}\, p^*(r_{ee})\, dr_{ee}}{\int_{r_{ee}=0}^{+\infty} p^*(r_{ee})\, dr_{ee}}$$

; let's momentarilly write 'r' instead of 'ree' for the sake of [clarity.

- $\int_0^{+\infty} r\, p^*(r)\, dr = 4\pi\left(2\pi\sigma^2\right)^{-3/2}\int_0^{+\infty} r^3 \exp\left(\frac{-r^2}{2\sigma^2}\right) dr$, which we integrate by parts:

$$= 4\pi\left(2\pi\sigma^2\right)^{-3/2}\left\{\left[-\sigma^2 r^2 \exp\left(\frac{-r^2}{2\sigma^2}\right)\right]_0^{+\infty} + 2\sigma^2\int_0^{+\infty} r \exp\left(\frac{-r^2}{2\sigma^2}\right) dr\right\}$$

$$= 4\pi\left(2\pi\sigma^2\right)^{-3/2}\left[-2\sigma^4 \exp\left(\frac{-r^2}{2\sigma^2}\right)\right]_0^{+\infty} = \left(\frac{8}{\pi}\right)^{1/2} \sigma^{5/2}$$

- $\int_0^{+\infty} p^*(r)\, dr = 4\pi\left(2\pi\sigma^2\right)^{-3/2}\int_0^{+\infty} r^2 \exp\left(\frac{-r^2}{2\sigma^2}\right) dr = 4\pi\left(2\pi\sigma^2\right)^{-3/2}\left\{\left[-r\sigma^2 \exp\left(\frac{-r^2}{2\sigma^2}\right)\right]_0^{+\infty} + \sigma^2\int_0^{+\infty}\exp\left(\frac{-r^2}{2\sigma^2}\right) dr\right\}$

$$= 4\pi\left(2\pi\sigma^2\right)^{-3/2} \sigma^2 . \frac{\sigma}{2}\sqrt{2\pi} = \sigma^{3/2}$$

$$\langle r_{ee}\rangle = \left(\frac{8}{\pi}\right)^{1/2} \sigma^{5/2} . \sigma^{-3/2} = \left(\frac{8\sigma^2}{\pi}\right)^{1/2} = \underline{\underline{\left(\frac{8}{3\pi}\right)^{1/2} N^{1/2}\, b}}$$

Problem 2 - Entropic elasticity of a 1-D polymer chain model

Freely jointed chain model in 1 D

a) Probability of a given conformation $p(\sigma_1, \dots, \sigma_N) = \frac{1}{Q'} \exp\left(\frac{-U(\sigma_1, \dots, \sigma_N)}{kT}\right) \exp\left(\frac{\underline{f} \cdot z\, \underline{e}}{kT}\right)$

where $U(\sigma_1, \dots, \sigma_N)$ is the internal energy of the system in the $\{\sigma_1, \dots, \sigma_N\}$ configuration

$U(\sigma_1, \dots, \sigma_N) = 0$ in the FJC model

$\underline{e}$ is the unit vector of the 1-D space

$\underline{f}$ and $z\underline{e}$ are colinear in a 1-D space, thus $\underline{f} \cdot z\underline{e} = fz = fb \sum_{i=1}^{N} \sigma_i$

and where $Q' = \int_{\text{phase space}} \exp\left(\frac{fb \sum_{i=1}^{N} \sigma_i}{kT}\right)$, under the assumption that $U_{\text{any microstate}} = 0$.

Here, the phase space is the ensemble of all possible arrangements of σ_i, $i \in [\![1, N]\!]$, each of the σ_i s being either 1 or -1

$$Q' = \int_{\forall i \in [\![1,N]\!],\ \sigma_i = -1 \text{ or } 1} \exp\left(\frac{fb}{kT}\sigma_1\right) \exp\left(\frac{fb}{kT}\sigma_2\right) \dots \exp\left(\frac{fb}{kT}\sigma_N\right)$$

Each exponential factor is actually identical, for no correlation exists from one segment to another one

$$Q' = \left[\exp\left(\frac{fb}{kT}\right) + \exp\left(\frac{-fb}{kT}\right)\right] \cdot \left[\exp\left(\frac{fb}{kT}\right) + \exp\left(-\frac{fb}{kT}\right)\right] \dots \left[\exp\left(\frac{fb}{kT}\right) + \exp\left(\frac{-fb}{kT}\right)\right]$$

$$= \left[\exp\left(\frac{fb}{kT}\right) + \exp\left(\frac{-fb}{kT}\right)\right]^N$$

$$\boxed{p(\sigma_1, \dots, \sigma_N) = \frac{1}{\left[\exp\left(\frac{fb}{kT}\right) + \exp\left(\frac{-fb}{kT}\right)\right]^N} \cdot \exp\left(\frac{fb}{kT} \sum_{i=1}^{N} \sigma_i\right)}$$

b) Force / extension behavior of a 1-D FJC

$\langle z \rangle = \frac{1}{Q'} \int_{\text{phase space}} z(\sigma_1, \dots, \sigma_N)\, p(\sigma_1, \dots, \sigma_N) = kT \frac{\partial}{\partial f} \ln Q'$, where $z(\sigma_1, \dots, \sigma_N) = b \sum_{i=1}^{N} \sigma_i$

From the expression for Q' in a), we have $\langle z \rangle = kT \frac{\partial}{\partial f} \ln \left\{\left[\exp\left(\frac{fb}{kT}\right) + \exp\left(\frac{-fb}{kT}\right)\right]^N\right\}$

$\langle z \rangle = NkT \cdot \frac{1}{e^x + e^{-x}} \cdot \frac{\partial}{\partial f}\left(e^x + e^{-x}\right)$ where $x = \frac{fb}{kT}$

$= NkT \cdot \frac{b}{kT} \cdot \frac{e^x - e^{-x}}{e^x + e^{-x}}$, which we can write again $\boxed{\frac{\langle z \rangle}{Nb} = \tanh\left(\frac{fb}{kT}\right)}$

c) Small force limit : for $f \ll \frac{kT}{b}$ and $x = \frac{fb}{kT}$, $e^x \sim 1 + x$

$\langle z \rangle \sim Nb \frac{(1+x) - (1-x)}{(1+x) + (1-x)} = Nbx$

1D · $\langle z \rangle \longrightarrow \frac{fb}{kT} Nb$

A spring constant (defined through entropic reasoning) would be defined as $k_{1D} = \frac{f}{\langle z \rangle}$.

$\boxed{k_{1D} = \frac{kT}{Nb^2} = \frac{1}{3} k_{3D}}$ (see class notes where in 3D $|\langle z \rangle| \longrightarrow \frac{1}{3} \frac{fb}{kT} Nb$)

d) One could anticipate the spring constant for the small force limit of a 2D FJC model to be $k_{2D} = 2 \frac{kT}{Nb^2}$.

Problem set # 2 - SOLUTION

Problem 4 - DNA folding

a) Free energy variations

From class notes, the free energy A can be expressed in terms of the partition function Q:
$A = -k_B T \ln Q$

Consider the two macrostates "hairpin" & "random"

$$\begin{cases} P_{hairpin} = \dfrac{Q_{hairpin}}{Q} \\ P_{random} = \dfrac{Q_{random}}{Q} \end{cases}$$

Hence
$$\frac{P_{hairpin}}{P_{random}} = \frac{Q_{hairpin}}{Q_{random}} = \exp\left(\frac{-(A_{hairpin} - A_{random})}{k_B T}\right)$$

$$\boxed{A_{hairpin} - A_{random} = -k_B T \ln\left(\frac{P_{hairpin}}{P_{random}}\right)}$$

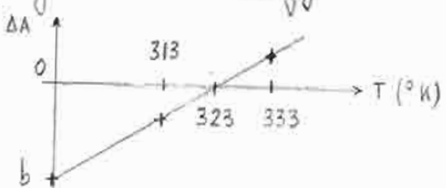
Temperature (°C)	$P_{hairpin}$	$\frac{P_{hairpin}}{P_{random}}$	$A_{hairpin} - A_{random}$ (J)	
40	0.87	6.69	$-8.2 \cdot 10^{-21}$ J	$(\simeq -2 k_B T)$
50	0.5	1	0	
60	0.13	0.15	$+8.7 \cdot 10^{-21}$ J	$(\simeq +2 k_B T)$

b) When T increases by 10 °K (= 10 °C), ΔA increases by $2 k_B T$ (or $\simeq 50$ kJ.mol^{-1}).

$$\left.\begin{aligned} A_{hairpin} &= U_{hairpin} - T S_{hairpin} \\ A_{random} &= U_{random} - T S_{random} \end{aligned}\right\} \quad \Delta A = \underbrace{(U_{hairpin} - U_{random})}_{(i)} - T\underbrace{(S_{hairpin} - S_{random})}_{(ii)}$$

(i) from base-pairing (ii) number of accessible configurations changes

(i) change in internal energy



intersect $\Delta U = -T_{\Delta A=0} \cdot \text{slope} = -(273+50)\dfrac{8.2 \cdot 10^{-21}}{10}$
$= -2.65 \cdot 10^{-19}$ J

and corresponds to the formation of 14 base pairs

Therefore $\Delta U_{base-pairing} = \dfrac{-2.65 \cdot 10^{-19}}{14} = -18.9 \cdot 10^{-21}$ J $= \underline{-4.4\ k_B T}$

(ii) Ratio of accessible configurations

$S_{hairpin} - S_{random} = -\text{slope} = -8.2 \cdot 10^{-22}$ J.K^{-1} $= k_B(\ln W_{hairpin} - \ln W_{random}) = k_B \ln \dfrac{W_{hairpin}}{W_{random}}$

$\dfrac{W_{hairpin}}{W_{random}} = \exp^{-\text{slope}/k_B} = 1.6 \cdot 10^{-26}$

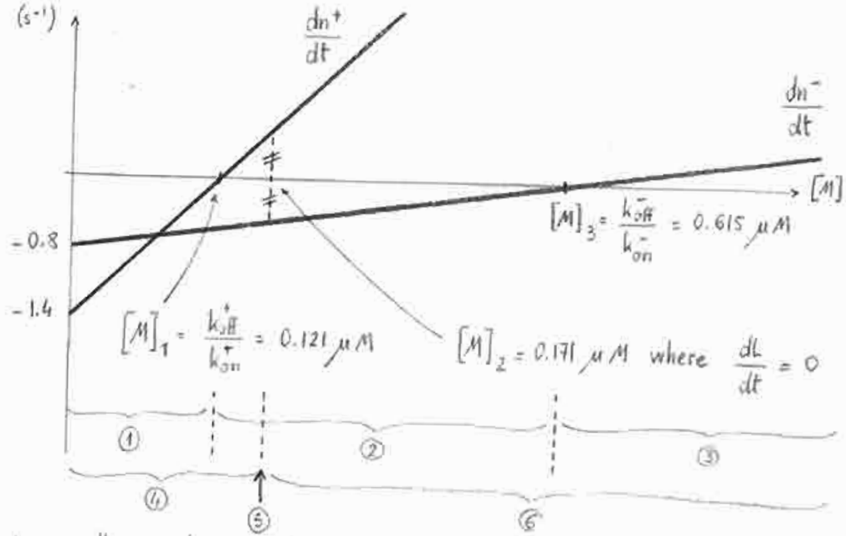
The hairpin configuration allows much fewer arrangements than the random one, but is favored energetically.

Problem 5 - Dynamics of actin polymerization

a) Three regimes of growth for the filament

$$\begin{cases} \dfrac{dn^+}{dt} = k_{on}^+ [M] - k_{off}^+ \\ \dfrac{dn^-}{dt} = k_{on}^- [M] - k_{off}^- \end{cases}$$

$$\frac{dL}{dt} = \frac{dn^+}{dt} + \frac{dn^-}{dt}$$



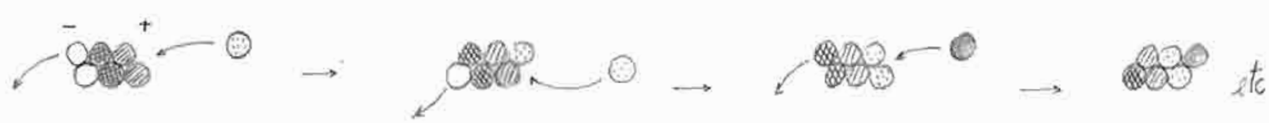
One can choose to define

- regimes ①, ② and ③
  - ① $0 < [M] < [M]_1$, $\frac{dn^+}{dt} < 0$ and $\frac{dn^-}{dt} < 0$ } shrinkage at both ends
  - ② $[M]_1 < [M] < [M]_3$, $\frac{dn^+}{dt} > 0$ and $\frac{dn^-}{dt} < 0$ } growth at ⊕ end, collape at ⊖ end; depending on the relative velocities, the length of the filament can increase, decrease or remain constant ($\frac{dL}{dt} = 0$ at $[M] = [M]_2$)
  - ③ $[M] > [M]_3$, $\frac{dn^+}{dt} > 0$ and $\frac{dn^-}{dt} > 0$ } elongation at both ends
- or regimes ④, ⑤, ⑥
  - ④ $\frac{dL}{dt} < 0$ shrinkage of filament
  - ⑥ $\frac{dL}{dt} > 0$ elongation " "
  - ⑤ $\frac{dL}{dt} = 0$ stationary regime, constant length for the actin filament

b) Treadmilling

Total length of filament constant in time if $\frac{dn^+}{dt} = -\frac{dn^-}{dt}$ (or $\frac{dL}{dt} = 0$)

$$\boxed{[M]_{treadmilling} = \frac{k_{off}^+ + k_{off}^-}{k_{on}^+ + k_{on}^-} = 0.171\ \mu mol.\ L^{-1}}$$



c) Velocity of treadmilling

$\left.\frac{dn^+}{dt}\right|_{treadmilling} = k_{on}^+ [M]_{treadmilling} - k_{off}^+ = 0.578$ actin monomer per second

Adding one actin monomer increases the length of the F-actin by $\frac{5,5}{2} = 2.75$ nm, thus the leading edge moves forward at $0.578 * 2.75 = 1.59\ nm.s^{-1} \ll 100\ nm.s^{-1}$ for keratocytes

Problem 5 (cont'd)

d) Taking into account severing proteins

Severing proteins can increase k^-_{off} by 2 orders of magnitude. Take $k^-_{off} = 100\, k^-_{off/initial} = 80\ s^{-1}$, and let the other constants remains the same.

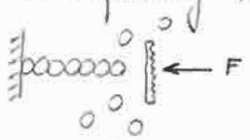
Now $[M]_{\substack{\text{treadmilling with}\\ \text{severing proteins}}} = 6.31\ \mu M$ and $\left.\dfrac{dn^+}{dt}\right|_{\substack{\text{treadmilling with}\\ \text{severing proteins}}} = 71.8\ s^{-1}$ or $\underline{197\ nm.s^{-1}}$

Severing proteins increase the velocity of treadmilling.

e) In class we have derived two relations:

- $$\boxed{F_{eq} = \frac{kT}{\delta} \ln\left(\frac{[M]}{K_c}\right)} \quad (1)$$ where $\begin{cases} \delta: & \text{length change in the filament when monomer added} \\ [M]: & \text{concentration of monomers} \\ K_c: & \text{critical dissociation constant} \end{cases}$

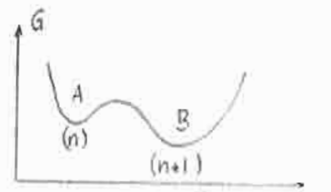
(1) describes the following situation:



F is the force required to stall the growth of the filament

(1) describes an equilibrium.

- $$\boxed{v = \frac{2D}{\delta}}$$ where D is the diffusion coefficient of monomers



n = number of monomers in a filament

(2) describes the same process, from a kinetic point of view.

(1) would give us information about the ratio of states A & B (filament with n & n+1 monomers respectively), while (2) provides information about the energy barrier the 2 states (information given by reaction rates).

- For actin pushing a particle $\begin{cases} D = \dfrac{kT}{\xi} \\ \xi = 6\pi\, \mu\, a \end{cases}$ radius of particle; viscosity of medium (take water)

take $\begin{cases} k = 1.38 \cdot 10^{-23}\ J.K^{-1} \\ T = 310\ ^\circ K \text{ (human body)} \\ \mu = 800 \cdot 10^{-6}\ Ns.m^{-2} \\ \delta = 2.75\ nm \end{cases}$

$$v = \frac{2D}{\delta} = \frac{2kT}{6\pi\, \mu a\, \delta} = \frac{kT}{3\pi\, \mu a\, \delta}$$

for $a = 10\ \mu m$,	$v \simeq 20\ \mu m.s^{-1}$
$a = 100\ \mu m$,	$v \simeq 2\ \mu m.s^{-1}$